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SCANNING THE LITERATURE

Summaries of Key Journal Articles

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Arrhythmias

Yield of Diagnostic Tests in Evaluating Syncopal Episodes in Older Patients

Mendu ML, McAvay G, Lampert R, Stoehr J, Tinetti ME.
***Arch Intern Med* 2009;169:1299–1305.**

Study Design: How useful are diagnostic tests for syncope in patients over the age of 65 years?

Methods: The subjects of this retrospective review were 2,106 patients (mean age 79 years) who underwent inpatient evaluation for syncope.

Results: The most common etiologies for syncope were: unknown, 47%; vasovagal, 22%; orthostatic hypotension, 13%; and arrhythmia, 12%. The most commonly performed diagnostic tests were: electrocardiogram, 99%; telemetry, 95%; cardiac enzymes, 95%; head computed tomography (CT), 63%; echocardiogram, 39%; and postural blood pressure (BP) recording, 38%. Postural BPs had the highest diagnostic yield (18-26%); other tests, 0.5-5%. The cost per cardiac test affecting the diagnosis was significantly lower when testing was limited to high-risk patients with heart failure, hematocrit <30%, an abnormal electrocardiogram, dyspnea, or a systolic BP <90 mm Hg.

Conclusions: Many elderly patients with syncope undergo unnecessary testing. Testing that is based on the history and initial clinical evaluation improves the cost-effectiveness of diagnostic testing for syncope.

Perspective: The most common cause of syncope in patients of all age groups is vasovagal syncope, which often can be reliably diagnosed based only on the description of circumstances, prodromal symptoms, and residual symptoms. Other than the history, the most helpful diagnostic test for vasovagal syncope is head-up tilt. Unfortunately, in this study, the diagnostic value of neither was evaluated.

Summary written by: Fred Morady, MD

Systematic Review: Comparative Effectiveness of Radiofrequency Catheter Ablation for Atrial Fibrillation

Terasawa T, Balk EM, Chung M, et al.
***Ann Intern Med* 2009;151:191–202.**

Study Design: How effective is radiofrequency catheter ablation (RFCA) of atrial fibrillation (AF)?

Methods: This was a review of 67 cohort studies, 32 randomized controlled trials, and 9 nonrandomized comparative studies published in 2000-2008 describing results of RFCA of AF with an 8-mm-tip or irrigated-tip ablation catheter, with at least 6 months of follow-up.

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Results: RFCA as second-line therapy was 3.46 times more likely to maintain sinus rhythm compared to drug therapy. One randomized study reported that RFCA as first-line therapy resulted in freedom from AF over 12 months more often than drug therapy (88% vs. 37%). A low strength of evidence suggests that there is not a significant difference between RFCA and drug therapy in improvement in ejection fraction or left atrial size, or in the stroke rate at 12 months. Evidence also suggests that RFCA improves quality of life, promotes avoidance of anticoagulation, and decreases rehospitalizations to a greater degree than drug therapy.

Conclusions: RFCA is more effective than medical therapy for preventing recurrences of AF.

Perspective: Most studies on RFCA of AF are cohort studies of relatively low scientific quality. At least two large-scale randomized clinical trials of RFCA versus drug therapy are currently in progress. However, the optimal ablation strategy (particularly for persistent AF) is as yet unclear, and ablation tools continue to evolve, making catheter ablation of AF a 'moving target.'

Summary written by: Fred Morady, MD

Cardiovascular Surgery

Percutaneous Mitral Annuloplasty for Functional Mitral Regurgitation: Results of the CARILLON Mitral Annuloplasty Device European Union Study

Schofer J, Siminiak T, Haude M, et al.
Circulation 2009;120:326–333.

Study Design: What is the feasibility and outcome of percutaneous mitral annuloplasty?

Methods: This was a single-arm evaluation of percutaneous mitral annuloplasty performed via the coronary sinus with the CARILLON Mitral Contour System. Patients with dilated cardiomyopathy, moderate to severe functional mitral regurgitation (MR), an ejection fraction <40%, and a 6-minute walk distance between 150 and 450 m were enrolled in the study. Outcome measures were echocardiographic MR grade, exercise tolerance, New York Heart Association class, and quality of life, and they were assessed at baseline and 1 and 6 months.

Results: The study enrolled 48 patients, of whom 18 did not receive the device. Of the 18 patients who did not get successfully treated, 3 had coronary sinus perforation or dissection, whereas in 13 patients, the device was recaptured due to slippage of the distal anchor (n = 3) and coronary artery compromise or insufficient reduction in MR (n = 10). One patient died during follow-up and there were three myocardial infarctions in the periprocedural phase. The major adverse event rate was 13% at 30 days. At 6 months, the severity of MR reduction on quantitative echocardiographic measures ranged from 22% to 32%. There was significant improvement in the 6-minute walk distance.

Conclusions: The study demonstrates safety, efficacy, and feasibility of percutaneous mitral annuloplasty.

Perspective: This is a rapidly evolving field, and further refinement in the device and better preprocedural imaging will further improve safety and reduce unsuccessful procedures. Larger controlled studies will be warranted to confirm clinical improvement and assess long-term implications of percutaneous mitral annuloplasty before it can be used in routine clinical practice.

Summary written by: Hitinder S. Gurm, MD

Congenital Heart Disease

Twenty-Five-Year Outcome of Pediatric Coronary Artery Bypass Surgery for Kawasaki Disease

Kitamura S, Tsuda E, Kobayashi J.
Circulation 2009;120:60–68.

Study Question: What is the long-term outcome of pediatric coronary artery bypass for patients with severe inflammatory coronary sequelae due to Kawasaki disease?

Methods: A retrospective review was performed at a single referral center. Indications for surgery included angiographically significant coronary lesions with stenosis of ≥75%, presence of clinical signs of myocardial ischemia, or positive signs of ischemia by exercise or pharmacological stress. Prior myocardial infarction was also considered an indication for surgical intervention.

Results: A total of 114 patients (median age 10, range 1-19 years) underwent surgery and were followed for a median of 19 years. The mean number of distal anastomoses was 1.7 ± 0.8 per patient, with the vast majority (111) involving the internal thoracic artery, with 24 patients receiving saphenous vein grafts. Both 20- and 25-year survival rates were 95%. There were five deaths, all sudden, except for a late

death after cardiac transplantation. Cardiac event rates were 67% at 20 years and 60% at 25 years, the majority being percutaneous coronary intervention and reoperation. The 20-year patency rate was 87% for internal thoracic artery grafts, and 44% for saphenous vein grafts.

Conclusions: The 25-year survival is excellent after coronary bypass for Kawasaki disease, although there is a significant need for re-intervention. The internal thoracic artery grafts performed best.

Perspective: Overall, surgical or percutaneous intervention for Kawasaki disease is rare and is required only for the most severe cases. The take-home message from this paper includes the overall safety and efficacy of coronary bypass in Kawasaki disease, the important role for the use of the internal mammary artery, and the necessity for lifetime follow-up because of the likely need for re-intervention.

Summary written by: Timothy B. Cotts, MD

General Cardiology

Association of Cytochrome P450 2C19 Genotype With the Antiplatelet Effect and Clinical Efficacy of Clopidogrel Therapy

Shuldiner AR, O'Connell JR, Bliden KP, et al.
***JAMA* 2009;302:849–857.**

Study Question: What gene variants are associated with reduced platelet response to clopidogrel therapy and increased coronary events following percutaneous coronary intervention (PCI)?

Methods: Clopidogrel was administered for 7 days to 429 healthy Amish persons and followed by ex vivo platelet aggregometry. A genome-wide association study was performed, followed by genotyping the loss-of-function cytochrome P450 (CYP) *2C19*2* variant (rs4244285). These findings were extended by examining the relation of the *CYP2C19*2* genotype to platelet function and cardiovascular outcomes in an independent sample of 227 patients undergoing PCI.

Results: Platelet response to clopidogrel was highly heritable ($h^2 = 0.73$; $p < 0.001$). Thirteen single-nucleotide polymorphisms (SNPs) on chromosome 10q24 within the *CYP2C18–CYP2C19–CYP2C9–CYP2C8* cluster were associated with diminished clopidogrel response. The rs12777823 polymorphism was in strong linkage disequilibrium with the *CYP2C19*2* variant, and was associated with diminished clopidogrel response, accounting for 12% of the variation in platelet aggregation to ADP. The relation between *CYP2C19*2* genotype and platelet aggregation was replicated in clopidogrel-treated patients undergoing coronary intervention ($p = 0.02$). Patients with the *CYP2C19*2* variant were more likely (20.9% vs. 10.0%) to have a cardiovascular ischemic event or death during 1 year of follow-up.

Conclusions: *CYP2C19*2* genotype was associated with diminished platelet response to clopidogrel treatment and poorer cardiovascular outcomes.

Perspective: This study extends previous work that polymorphisms in these enzymes, leading to reduced enzyme activity, blunt the platelet and clinical response to clopidogrel. SNP genotyping may be useful in determining appropriate pharmacotherapy for patients with acute coronary syndromes and those following stenting. The appropriate alternative treatment (higher clopidogrel dose or another thienopyridine) for patients testing positive will need to be determined in future studies. Alternatively, use of drugs that do not require bioconversion, as standard initial treatment, could eliminate the need for genotyping.

Summary written by: Daniel T. Eitzman, MD

Assessment of Aspirin Resistance Varies on a Temporal Basis in Patients With Ischaemic Heart Disease

Muir AR, McMullin MF, Patterson C, McKeown PP.
***Heart* 2009;95:1225–1229.**

Study Question: What is the prevalence of aspirin resistance in patients with ischemic heart disease, and what is the concordance and repeatability of tests to detect aspirin resistance?

Methods: The authors enrolled 172 patients and measured platelet function at baseline, 1 week, and 2 weeks later. Aspirin-induced platelet inhibition was assessed using optical platelet aggregometry (OPA), platelet function analyser (PFA-100), and serum and urinary thromboxane B_2 (TXB_2) metabolite levels.

Results: One week after starting aspirin, 1.7% of patients were aspirin resistant by OPA and 22.1% by PFA-100. At 2 weeks, 4.7% were aspirin resistant by OPA, and 20.3% by PFA-100. There were poor correlations between PFA-100 and OPA, and between TXB_2 metabolites and platelet function tests. Levels of TXB_2 metabolites and measures of

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platelet function demonstrated marked variability between the two visits, suggesting that aspirin resistance is not predictable over time.

Conclusions: The prevalence of aspirin resistance is dependent on the method of testing, and there is significant variation in the antiplatelet effect of aspirin, as measured by these assays.

Perspective: Some literature suggests worse outcome in patients with aspirin resistance, although the strength varies based on the assay used. There is no consensus on what defines platelet resistance to aspirin, and this study shows little correlation between different assays in defining aspirin-resistant versus aspirin-sensitive state. Currently, no good data support routine evaluation for aspirin resistance in daily clinical practice.

Summary written by: Hitinder S. Gurm, MD

Perioperative Safety in the Longitudinal Assessment of Bariatric Surgery

Flum DR, Belle SH, King WC, et al., on behalf of the Longitudinal Assessment of Bariatric Surgery (LABS) Consortium.
***N Engl J Med* 2009;361:445–454.**

Study Question: What are the risks and risk factors associated with bariatric surgical procedures?

Methods: A prospective, multicenter, observational study of 30-day outcomes was conducted in consecutive patients undergoing bariatric surgical procedures at 10 clinical sites in the United States from 2005 through 2007. A composite endpoint of 30-day major adverse outcomes was evaluated.

Results: There were 4,776 patients who had a first-time bariatric procedure (mean age, 44.5 years; 21.1% men median body mass index [BMI], 46.5 kg/m^2). At least one coexisting condition was present in 82.1%, 53.9% had two or more, and 26.5% had three or more. The most common were hypertension (55.1%), obstructive sleep apnea (48.9%), diabetes (33.2%), and asthma (23.1%). A Roux-en-Y gastric bypass was performed in 3,412 patients (87.2% performed laparoscopically), and laparoscopic adjustable gastric banding was performed in 1,198 patients; 166 patients underwent other procedures and were not included in the analysis. The 30-day rate of death among patients who underwent a Roux-en-Y gastric bypass or laparoscopic adjustable gastric banding was 0.3%; 4.3% of patients had at least one major adverse outcome.

Conclusions: The overall risk of death and adverse outcomes after bariatric surgery was low and varied considerably according to patient characteristics. In helping patients make appropriate choices, short-term safety, long-term effects of bariatric surgery, and the risks associated with being extremely obese should be considered.

Perspective: The morbidity and mortality of bariatric surgery is considerably less than in original reports, and quality of life continues to improve. The relatively short-term (few years) results include major weight loss, improved exercise capacity, improved blood pressure and glycemic control, and improved quality of life. Guidelines now support having bariatric surgery in the morbidly obese and in those with diabetes or multiple risk factors with a BMI >35 kg/m^2.

Summary written by: Melvyn Rubenfire, MD

Sex Differences in Mortality Following Acute Coronary Syndromes

Berger JS, Elliott L, Gallup D, et al.
***JAMA* 2009;302:874–882.**

Study Question: Do sex-related differences exist in mortality after acute coronary syndromes (ACS)?

Methods: A convenience sample of patients from 11 independent randomized ACS clinical trials was used for the analysis. Trials were conducted between 1993 and 2006. Patients were grouped by ACS type: unstable angina (UA), ST-elevation myocardial infarction (STEMI), and non-STEMI (NSTEMI). The primary outcome of interest was 30-day mortality

Results: A total of 136,247 patients were included; 28% were women. For those with STEMI, 26% were women, for NSTEMI 29% were women, and for UA 40% were women. Overall, 30-day mortality was 9.6% for women and 5.3% for men. For ACS, among STEMI patients, women were more likely to experience 30-day mortality. Women with NSTEMI had lower mortality rates and UA. In a cohort of patients (n = 35,128) with angiographic data, women were more likely to have nonobstructive coronary artery disease (15% vs. 8%), and less likely to have two- (25% vs. 28%) and three-vessel coronary disease (23% vs. 26%), regardless of ACS type. After adjustment for angiographic disease severity, no differences in 30-day mortality were observed between men and women, regardless of ACS type.

Conclusions: Differences in 30-day mortality rates between men and women differed between ACS types, largely

explained by clinical differences at presentation and disease severity.

Perspective: These findings suggest that differences in short-term mortality after ACS may be related to coronary artery disease severity, rather than sex.

Summary written by: Elizabeth A. Jackson, MD

Heart Failure/Transplant

Percutaneous Left Ventricular Assist Devices vs. Intra-Aortic Balloon Pump Counterpulsation for Treatment of Cardiogenic Shock: A Meta-Analysis of Controlled Trials

Cheng JM, den Uil CA, Hoeks SE, et al.
***Eur Heart J* 2009;Jul 18:[Epub ahead of print].**

Study Question: What are the potential benefits of percutaneous left ventricular assist devices (LVADs) on hemodynamics and 30-day survival in patients with cardiogenic shock?

Methods: Two independent investigators searched for all controlled trials using percutaneous LVADs in patients with cardiogenic shock, where after data were extracted using standardized forms. Weighted mean differences for cardiac index, mean arterial pressure, and pulmonary capillary wedge pressure (PCWP) were calculated. Relative risks were calculated for 30-day mortality, leg ischemia, bleeding, and sepsis.

Results: After device implantation, percutaneous LVAD patients had higher cardiac index, higher mean arterial pressure, and lower PCWP compared with intra-aortic balloon pump (IABP) patients. Similar 30-day mortality was observed using percutaneous LVADs compared with IABPs. Bleeding was significantly more observed in TandemHeart patients compared with patients treated with IABP.

Conclusions: Although percutaneous LVADs provide superior hemodynamic support in patients with cardiogenic shock compared with IABPs, the use of these more powerful devices did not improve early survival. Results do not yet support percutaneous LVADs as a first-choice approach in the mechanical management of cardiogenic shock.

Perspective: The key take-home message is that the percutaneous LVADs are associated with better hemodynamics. Until recently, most centers have used percutaneous LVADs for sicker patients. Direct comparisons between these newer devices with IABP are needed to determine their impact on survival.

Summary written by: Ragavendra R. Baliga, MBBS

Interventional Cardiology

Sirolimus-Eluting Stent Treatment at High-Volume Centers Confers Lower Mortality at 6-Month Follow-Up: Results From the Prospective Multicenter German Cypher Registry

Khattab AA, Hamm CW, Senges J, et al., on behalf of the German Cypher Registry.
***Circulation* 2009;120:600–606.**

Study Question: Is there a relation between institutional procedure volume and outcome in patients undergoing percutaneous coronary intervention (PCI) with the Cypher stent?

Methods: This was a secondary analysis of the German Cypher registry. The registry enrolled 8,201 patients treated with sirolimus-eluting stents (SES) between April 2002 and September 2005 in 51 centers. The authors categorized hospitals into those that recruited >400 patients as high-volume, 150-400 patients as intermediate-volume, and <150 patients as low-volume centers.

Results: Patients at low-volume centers were more likely to present with acute coronary syndrome (ACS) and be younger and diabetic. Low-volume centers used shorter and smaller diameter stents, and the deployment pressures were lower. Major cardiac adverse events occurred in 11.3%, 12.1%, and 9.0% of patients in the low-, intermediate-, and high-volume center groups, respectively. This gradient in outcome was observed both in patients with stable coronary artery disease (2.8%, 1.8%, and 1.2%) and ACS (6.0%, 3.9%, and 2.4%), respectively. Difference in death/myocardial infarction remained significant after adjustment for baseline factors.

Conclusions: Patients treated with SES stents at low-volume centers have a worse outcome.

Perspective: This study provides further support for mandating minimum procedure volume standards for institutions. A strong argument is often made in the name of patient convenience for expanding elective PCI to sites with no surgical backup. Although the need for surgical backup is infrequent, expanding PCI to more centers could replace a few high-

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volume centers with multiple low-volume centers, and potentially lead to a decrease in safety and quality of care.

Summary written by: Hitinder S. Gurm, MD

The Dissociation Between Door-to-Balloon Time Improvement and Improvements in Other Acute Myocardial Infarction Care Processes and Patient Outcomes

Wang TY, Fonarow GC, Hernandez AF, et al.
Arch Intern Med 2009;169:1411–1419.

Study Question: What is the correlation between improvement in specific targeted quality measures (such as door-to-balloon [DTB] time) and other quality measures and outcomes?

Methods: The authors studied the association between improvement in D2B time at 101 hospitals participating in the Get With the Guidelines program from 2005 to 2007 with changes in composite Centers for Medicare and Medicaid Services/Joint Commission on Accreditation of Healthcare Organizations (CMS/JCAHO) core measure performance and in-hospital mortality.

Results: The mean D2B time decreased from 101 to 87 minutes, whereas hospital composite CMS/JCAHO core measure performance increased from 93.4% to 96.4%. Mortality rates declined from 5.1% to 4.7%. There was no correlation between improvement in hospital D2B time and changes in composite quality performance or in-hospital mortality. Lack of association between these measures persisted after adjustment for differences in patient mix.

Conclusions: Within the Get With the Guidelines program, there was no correlation between DTB time improvement and changes in other quality measures or mortality.

Perspective: Hospitals participating in the Get With the Guidelines program achieved remarkable improvement in the CMS/JCAHO core measures, with scores in the high 90s before the start of this study. It is plausible that a ceiling effect limited the magnitude of improvement in core measures while there was significant room for improvement in D2B time. This may have limited the ability to detect a possible association between improvements in the measures. More likely, the results of the study reflect the need for broader quality improvement efforts to achieve improvement in all aspects of health care delivery.

Summary written by: Hitinder S. Gurm, MD

Noninvasive Cardiology

Dramatic Reduction in Infective Endocarditis-Related Mortality With a Management-Based Approach

Botelho-Nevers E, Thuny F, Casalta JP, et al.
Arch Intern Med 2009;169:1290–1298.

Study Question: Does a standardized diagnostic and therapeutic protocol impact outcome among patients with infective endocarditis (IE), and does outcome correlate with compliance with the management-based protocol?

Methods: At a single tertiary care teaching hospital in France, an observational study was performed between 1991 and 2006 that included 333 consecutive patients treated for IE. The study was divided into two time periods: 1991 to 2001, before implementation of a standardized therapeutic protocol (173 patients); and 2002 to 2006, after implementation of the protocol (160 patients). The management protocol evaluated a sampling of biological specimens; and used only four antimicrobial agents with standardized duration of treatment, standardized surgical indications, and 1 year of close follow-up.

Results: The 1-year mortality decreased significantly from 18.5% during the initial period to 8.2% after initiation of the standardized protocol. After multivariable analysis, management with the standardized protocol remained a strong protective factor. During the latter period, there was significantly better compliance in antimicrobial therapy and fewer cases of renal failure. Deaths by embolic events and multiple organ failure also significantly decreased during the latter period.

Conclusions: A dramatic reduction in mortality was observed during the implementation of a standardized protocol for the management of IE, suggesting that a management-based approach has a significant impact on IE outcome.

Perspective: The study is of interest, and shows better compliance with appropriate antibiotic regimens, and improved outcomes after the implementation of a standardized protocol for management. This study supports consideration for more standardized approaches for IE management. In addition, there might be fertile ground for more standardized approaches to diagnosis of IE—despite the general acceptance of the modified Duke criteria, do we really need all those transesophageal echocardiograms to 'rule out' IE?

Summary written by: David S. Bach, MD

Subclinical Brain Embolization in Left-Sided Infective Endocarditis. Results From the Evaluation by MRI of the Brains of Patients With Left-Sided Intracardiac Solid Masses (EMBOLISM) Pilot Study

Cooper HA, Thompson EC, Laureno R, et al.
Circulation 2009;120:585–591.

Study Question: What is the actual incidence of acute brain embolization in patients with left-sided infective endocarditis (IE)?

Methods: A cohort of 56 patients with definite left-sided IE was prospectively studied. Patients were examined by a neurologist, and those without contraindication had magnetic resonance imaging (MRI) of the brain. Patients without clinical evidence of acute stroke, but with MRI evidence of acute brain embolization, were considered to have subclinical brain embolization.

Results: Clinical stroke was present in 25% of patients. Among 40 patients undergoing MRI, incidence rates of subclinical and any acute brain embolization were 48% and 80%, respectively. Acute brain embolization was present in 95% of patients with *Staphylococcus aureus* infection. At 3 months, mortality was similar among patients with clinical stroke and subclinical brain embolization, and was higher among patients with any acute brain embolization than those without. Valvular surgery was performed in 25 patients (45%), including 16 with acute brain embolization, at a median of 4 days. Surgery was independently associated with a lower risk of mortality at 3 months.

Conclusions: MRI detected subclinical brain embolization in a substantial number of patients with left-sided IE, suggesting that the incidence of acute brain embolization may be significantly higher than reports based on clinical and computed tomography (CT) findings have indicated. Brain MRI may play a role in the complex decision about surgical intervention in IE.

Perspective: This is a provocative study, suggesting that subclinical brain embolization commonly complicates left-sided IE. Among 40 patients without clinical evidence of stroke, MRI revealed evidence of acute brain embolization in 80%. Additional study may be required to sort out whether MRI evidence of acute brain embolization is an indication, or a contraindication, to early surgery in patients with active left-sided IE.

Summary written by: David S. Bach, MD

Prevention/Vascular

Apixaban or Enoxaparin for Thromboprophylaxis After Knee Replacement

Lassen MR, Raskob GE, Gallus A, Pineo G, Chen D, Portman RJ.
N Engl J Med 2009;361:594-604.

Study Question: What is the safety and efficacy of a factor Xa inhibitor, apixaban, versus a low molecular weight heparin, enoxaparin, for thromboprophylaxis after major joint replacement surgery?

Methods: Subjects undergoing total knee replacement were randomized to 2.5 mg of apixaban orally daily, or 30 mg of subcutaneous enoxaparin twice daily, both started 12-24 hours after surgery and continued for 10-14 days. All subjects underwent bilateral venography, and the primary efficacy outcome was a composite of asymptomatic and symptomatic deep vein thrombosis, nonfatal pulmonary embolism, and death from any cause. Follow-up was for 60 days.

Results: Of 3,195 patients who underwent randomization, 908 subjects were not eligible for efficacy analysis, although all but 11 subjects were included in the safety analysis. The overall rate of primary outcome events was much lower than expected, with the rate of primary efficacy outcome of 9.0% and 8.8% in the apixaban and enoxaparin groups, respectively. The composite incidence of major bleeding or clinically relevant nonmajor bleeding was 2.9% versus 4.3% with apixaban and enoxaparin, respectively.

Conclusions: For efficacy of thromboprophylaxis after knee replacement surgery, a comparison of enoxaparin and apixaban did not meet prespecified statistical criteria for noninferiority. Use of apixaban was associated with lower rates of clinically relevant bleeding, and it had a similar adverse event profile.

Perspective: Despite planning to use venography in all subjects, this study suffered from a lower than expected number of outcomes, rendering it underpowered to answer the study question. Although this study provides some hope that factor Xa inhibitors may prove as efficacious and yet safer than low molecular weight heparin, there remains significant controversy as to the necessity of such aggressive thromboprophylaxis, even after high-risk surgery. Finding the ideal agent remains an elusive goal. The current study contributes to the hope that newer agents may bring us closer to that goal.

Summary written by: James B. Froehlich, MD

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Association of Cardiovascular Risk Factors With Mental Health Diagnoses in Iraq and Afghanistan War Veterans Using VA Health Care

Cohen BE, Marmar C, Ren L, Bertenthal D, Seal KH.
JAMA 2009;302:489-492.

Study Question: Are cardiovascular risk factors common among Iraq and Afghanistan war veterans with mental health disorders?

Methods: Data from the Veterans Administration (VA) roster were used to identify veterans who had access to VA health care from October 7, 2001 to September 30, 2008. Veterans were grouped by the presence of mental health diagnosis (no mental health diagnosis, mental health diagnosis with no post-traumatic stress disorder [PTSD]; and mental health diagnosis with PTSD). Sex-stratified, multivariate logistic regression was used to examine association of these groups with cardiovascular risk factors.

Results: A total of 303,223 veterans were included (mean age 31 years; 88% men). PTSD was common among the cohort (24%); among those, comorbid mental health conditions were prevalent including depression (53%), anxiety disorder (29%), adjustment disorder (26%), and alcohol use disorder (22%). Veterans with mental health diagnosis were more likely to have cardiovascular risk factors including tobacco use, hypertension, hyperlipidemia, and obesity compared to those without mental health disorders, after controlling for multiple factors.

Conclusions: Cardiovascular risk factors are common among veterans with mental health disorders.

Perspective: These findings suggest the critical need for risk factor modification and prevention among a young population of veterans. Whether risk factor modification with or without treatment of mental health disorders in this population will reduce cardiovascular events will need to be assessed in future prospective trials.

Summary written by: Elizabeth A. Jackson, MD

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Effect of Telmisartan on Renal Outcomes: A Randomized Trial

Mann JF, Schmieder RE, Dyal L, et al., on behalf of the TRANSCEND (Telmisartan Randomised Assessment Study in ACE Intolerant Subjects With Cardiovascular Disease) Investigators.
Ann Intern Med 2009;151:1-10.

Study Question: What are the long-term renal effects of telmisartan versus placebo in adults with cardiovascular disease?

Methods: The authors reported results of the TRANSCEND study, a randomized trial of telmisartan 80 mg/d versus placebo in subjects greater than age 55 with known coronary artery disease or diabetes mellitus and end-organ damage (but no microalbuminuria), who were intolerant of angiotensin-converting enzyme inhibitors. Prespecified renal outcome of dialysis, doubling of serum creatinine, death, as well as changes in glomerular filtration rate (GFR) and albuminuria were reported.

Results: Among 5,927 adults randomized to telmisartan (n = 2,954) or matching placebo (n = 2,972), there was no significant difference in the composite renal outcome (58 patients [1.96%] vs. 46 patients [1.55%] in the ARB and placebo groups, respectively). Serum creatinine doubled in 56 and 36 telmisartan and placebo patients, respectively. Fewer telmisartan than placebo patients had an increase in albuminuria (32% vs. 63%). GFR decreased significantly more in the telmisartan group than placebo (mean change in estimated GFR, -3.2 ml/min per 1.73 m^2 vs. -0.26 ml/min per 1.73 m^2).

Conclusions: In adults with vascular disease but without microalbuminuria, the effects of telmisartan on major renal outcomes were similar to those of placebo.

Perspective: This study suggests that angiotensin-receptor blocker (ARB) therapy in patients with vascular disease, but without evidence of nephropathy, does not prevent progression to renal dysfunction. Since the renal outcomes are of unclear clinical significance, but ARB use was associated with an improvement in cardiovascular outcomes, consideration for cardiovascular events should dominate decisions regarding use of these agents. This study provides no data supporting an expectation of ARB-associated improvement in renal outcomes in patients with vascular disease, but no nephropathy.

Summary written by: James B. Froehlich, MD